

# **Rotavirus Vaccine in Neonates**

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# **Rotavirus vaccination:**

## **Targeting neonates**

### **Background**

- **Infection in neonatal age is a natural way to acquire rotavirus in many areas of the world**
- **Subclinical infection in neonates protects against severe rotavirus disease in infancy**

**(Bishop et al, NEJM 1983;309:72-6)**

**(Bhan et al, JID 1993;168:282-7)**

## **Evaluation of RIT 4237 Bovine Rotavirus Vaccine in Newborn Infants: Correlation of Vaccine Efficacy to Season of Birth in Relation to Rotavirus Epidemic Period**

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## **Tampere 1984-1987**

**A single dose of bovine rotavirus vaccine RIT 4237 at the age of 5-7 days**

**A randomised, placebo-controlled trial**

**October 1984 group N=244,  
follow-up 2.8 years**

**June 1985 group N=245,  
follow-up 2.0 years**

## Serological responses to bovine rotavirus vaccine in 5-7 day-old infants

	<b>ELISA IgM</b>	<b>Neut</b>	<b>Both</b>
<b>Oct 84</b>			
<b>Vaccine</b>	<b>41 / 119 (35%)</b>	<b>35 / 115 (30%)</b>	<b>50 / 120 (42%)</b>
<b>Placebo</b>	<b>1 / 113 ( 1%)</b>	<b>0 / 113 ( 0)</b>	<b>1 / 113 ( 1%)</b>
<b>Jun 85</b>			
<b>Vaccine</b>	<b>30 / 123 (24%)</b>	<b>38 / 95 (40%)</b>	<b>46 / 95 (48%)</b>
<b>Placebo</b>	<b>1 / 105 ( 1%)</b>	<b>0 / 105 ( 0)</b>	<b>1 / 105 ( 1%)</b>

**Scand J Infect Dis 1990;22:269-78**

# Rotavirus gastroenteritis during follow-up

	<b>Vaccine</b>	<b>Placebo</b>
<b>Oct 84</b> <b>(F/u 2.8 yrs)</b>	<b>22</b>	<b>24</b>
<b>Jun 85</b> <b>(F/u 2 years)</b>	<b>18</b>	<b>16</b>
<b>Total</b>	<b>40</b>	<b>40</b>

# Protection against rotavirus gastroenteritis by severity (0-20 point score) Oct 84 Group

<b>Score</b>	<b>Vaccine</b>	<b>Placebo</b>	<b>Protection %</b>
<b><math>\geq 14</math></b>	<b>0</b>	<b>4</b>	<b>100 %</b>
<b><math>\geq 11</math></b>	<b>0</b>	<b>13</b>	<b>100 %</b>
<b><math>\geq 7</math></b>	<b>6</b>	<b>22</b>	<b>73 %</b>

# Protection against rotavirus gastroenteritis by severity (0-20 point score) Oct 85 Group

<b>Score</b>	<b>Vaccine</b>	<b>Placebo</b>	<b>Protection %</b>
<b><math>\geq 14</math></b>	<b>1</b>	<b>6</b>	<b>83 %</b>
<b><math>\geq 11</math></b>	<b>7</b>	<b>9</b>	<b>22 %</b>
<b><math>\geq 7</math></b>	<b>13</b>	<b>16</b>	<b>19 %</b>

# Protection against rotavirus gastroenteritis by severity, mean scores

<b>Group</b>	<b>Vaccine</b>	<b>Placebo</b>	
<b>Oct 84</b>	<b>4.5</b>	<b>10.7</b>	<b>p&lt;0.001</b>
<b>June 85</b>	<b>8.2</b>	<b>11.6</b>	<b>p=0.009</b>
<b>Both</b>	<b>6.2</b>	<b>11.2</b>	<b>p&lt;0.001</b>

## **Conclusions**

- 1. A single dose of bovine rotavirus vaccine in neonatal age gives significant protection against severe rotavirus gastroenteritis**
- 2. Vaccine efficacy is dependent on season**
  - high efficacy when given shortly before RV season**
  - low efficacy when time interval between dosing and RV season is long**

# **Conclusions**

- 3. Bovine rotavirus vaccine is less immunogenic in neonates than in older infants**
- 4. Bovine rotavirus vaccine is safe in neonates**

# **Rhesus rotavirus tetravalent (RRV-TV) vaccine in neonates**

**T. Vesikari, A. Karvonen, B.D. Forrest,  
A.Z. Kapikian**

**(unpublished)**

# **Rationale**

**RRV-TV causes febrile reactions**

**3-5 days post vaccination**

**In Finnish infants, febrile reactions seen in 30 of infants age 3 months after first dose of RRV-TV (3 % high fever)**

**(Connection between reactogenicity (fever) and intussusception ? Not an issue in 1997 when study was conducted)**

# **Study design**

**Randomised, double blind trial**

**Each infant was dosed at 0, 2, 4 and 6 months**

**Bleedings at 5 months and 7 months of age**

**Dosing schedules**

**Actual vaccine (months)**

**PL – RV – RV – RV**

**2 – 4 – 6**

**RV – PL – RV – RV**

**0 – 4 – 6**

**RV – RV – RV – PL**

**0 – 2 – 4**

# **Reactogenicity after RRV-TV**

**(Fever on days 3 to 5 post-vaccination)**

	<b>No. (%) with fever</b>
<b>Neonatal dose</b>	<b>0 / 62 ( 0 )</b>
<b>No neonatal dose</b> <b>(First dose at 2 months)</b>	<b>5 / 28 (18%)</b>

**p = 0.015**

# **Rotavirus IgA seroconversion at 7 months**

**RRV-TV  
Dosing**

**No. (%) with  
seroconversion**

**2 - 4 - 6**

**28 / 28 (100%)**

**0 - 4 - 6**

**28 / 31 ( 90%)**

**0 - 2 - 4**

**28 / 31 ( 90%)**

# **RRV-TV neutralizing antibody responses by 7 months of age**

**RRV-TV  
Dosing**

**No. (%) with  
responses**

**2 - 4 - 6**

**26 / 28 ( 93%)**

**0 - 4 - 6**

**28 / 29 ( 97%)**

**0 - 2 - 4**

**26 / 31 ( 84%)**

**Any evidence of serological response (=vaccine "take") after RRV-TV vaccination**

**Start at**

**Neonatal age 97 %**

**2 months of age 100 %**

# **Conclusions**

- 1. Administration of RRV-TV vaccine to neonates is safe, in terms of absence of febrile reactions**
- 2. Immunogenicity of RRV-TV vaccine in neonates is lower than in older infants**
- 3. Immunogenicity after 3 doses of RRV-TV at 0, 2, and 4 months of age is at least satisfactory**

# **Neonatal rotavirus vaccination**

## **General points**

**Neonatal age may be the safest period to administer a live attenuated oral rotavirus vaccine**

- **low reactogenicity**
- **low rate of naturally occurring intussusception**
- **low risk of vaccine associated intussusception**

# **Neonatal rotavirus vaccination**

## **General points**

- 1. Easy reach of target population even in developing countries  
(Administration of RV vaccine at the same time as BCG)**
- 2. Even a single dose might have a significant clinical impact by preventing severe rotavirus gastroenteritis later in infancy**